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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/421,971	10/20/1999	FRED H. GAGE	SALK2350	4863

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EXAMINER

MURPHY, JOSEPH F

ART UNIT

PAPER NUMBER

1646

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12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/421,971	GAGE ET AL.	
	Examiner	Art Unit	
	Joseph F Murphy	1646	

The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM

**A SHORTENED STATUTORY PERIOD FOR REPLY
TO THE MAILING DATE OF THIS COMMUNICATION.**

THE MAILING DATE OF THIS COMMUNICATION: Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication. If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely. If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication. Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) Responsive to communication(s) filed on 27 December 2001 .

2a) This action is **FINAL**. 2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4) Claim(s) 1-11 and 13-60 is/are pending in the application.
4a) Of the above claim(s) 23-51 and 55-60 is/are withdrawn from consideration.

5) Claim(s) _____ is/are allowed.

6) Claim(s) 1-11, 13-22 and 52-54 is/are rejected.

7) Claim(s) _____ is/are objected to.

8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on _____ is: a) approved b) disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) All b) Some * c) None of:
1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. ____.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) The translation of the foreign language provisional application has been received.

15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) Notice of References Cited (PTO-892) 4) Interview Summary (PTO-413) Paper No(s). _____ .
2) Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) Notice of Informal Patent Application (PTO-152)
3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ . 6) Other: _____ .

DETAILED ACTION

Formal Matters

1. Claim 18 was amended, and claim 12 was cancelled, in Paper No. 11, 12/27/2001.

Claims 1-11, 13-60 are pending. Claims 23-51, 55-60 are withdrawn from consideration pursuant to 37 CFR 1.142(b). Claims 1-11, 13-22, 52-54 are under consideration.

Claim Rejections - 35 USC § 112 first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Pending claims 1-11, 13-22, 52-54 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a chimeric protein comprising two functional units each comprising the dimerization domain of a steroid/thyroid hormone nuclear receptor superfamily with an optional linker wherein the receptor is an ecdysone receptor, a Usp receptor or a retinoid X receptor, does not reasonably provide enablement for a chimeric protein comprising two functional units each comprising the dimerization domain of a steroid/thyroid hormone nuclear receptor superfamily with an optional linker, where in the receptor is any other steroid/thyroid hormone nuclear receptor linker interposed, for reasons of record set forth in Paper No. 10, 8/23/2001. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The rejection is based upon the argument that claim 1 is overly broad in the recitation of "steroid/thyroid hormone nuclear receptor superfamily" since the Specification provides

insufficient guidance as to which of the myriad of fusion polypeptides encompassed by the claim will retain the functional characteristics such that it can be used as a non-mammalian based transcription regulating system (page 4, lines 11-18) which would require that it respond to application of hormone.

Applicant argues that the instant invention requires that the two functional protein units form a functional entity, which form a functional entity, and that the specification defines a functional entity as possessing the biological function of a dimer between two equivalent monomeric units. However, insufficient guidance is provided as to which of the myriad of polypeptide species encompassed by the claim will retain the desired characteristics because insufficient direction is provided regarding the relationship of the chimeras structure and its function, especially given the indefinite nature of the term "functional entity" (*infra*). The scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Although the specification states that these types of changes are routinely done in the art, the specification and claim do not provide any guidance as to what changes should be made.

3. Claims 52-54 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention.

Claims 52-54 are directed to an isolated protein crystal. However, it is commonly known in the art that production of protein crystals is difficult. There is insufficient guidance provided in the instant specification as to how one of ordinary skill in the art would generate an isolated protein crystal suitable for x-ray diffraction. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The Wands Court set forth eight factors to consider in the determination of whether a disclosure does not satisfy the enablement requirement and would require undue experimentation. The relevant factors in the instant case are set forth below:

- (1) the nature of the invention - the claimed invention is an isolated protein crystal suitable for x-ray diffraction.
- (2) the state of the prior art - the prior art teaches the difficulty of protein crystallization. As evidence, column 4, lines 23-44 of U.S. Patent No. 6,268,158 (Pantoliano et al.) discloses that crystallographic analysis remains difficult because there are not straightforward methodologies of obtaining X-ray quality protein crystals, and that conventional methods cannot be used to identify crystallization conditions that have the highest probability of promoting crystallization.
- (3) the level of one of ordinary skill the Panoliano disclosure is evidence that one of ordinary skill in the art would have difficulty making the crystal.
- (4) the level of predictability in the art - the Pantoliano disclosure is evidence that the level of predictability in making protein crystals is low.
- (5) the amount of direction provided by the inventor - the specification has provided insufficient guidance to make protein crystals based upon the disclosure of Pantoliano which

discloses that conventional methods of determining crystallization conditions are cumbersome, slow and labor intensive (column 4, lines 40-41).

(6) the existence of working examples - no working examples are provided.

(7) the quantity of experimentation needed to make or use the invention based on the content of the disclosure - Given the disclosure of Pantoliano, it would require undue experimentation to produce an isolated protein crystal suitable for x-ray diffraction, of the protein claimed in claim 1.

Given the nature of the invention, in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make the claimed invention.

Claim Rejections - 35 USC § 112 second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-11, 13-22, 52-54 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite in the recitation of the term "functional entity". There is no indication in the claim as to what function the protein must have. Therefore, the metes and bounds of the claim cannot be determined. Claims 2-11, 13-22, 52-54 are rejected insofar as they depend on the recitation in claim 1 of "functional entity".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

5. The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1-11, 13-22 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 6,265,173 (Evans et al.), which has a priority date of March 22, 1990.

Evans discloses multimeric receptor species that belong to the steroid/thyroid superfamily of receptors, comprising at least one member of the steroid/thyroid superfamily of receptors and the ultraspiracle receptor (column 3, lines 22-27). The multimeric receptors of Evans are disclosed as comprising a heterodimeric, heterotrimeric and heterotetrameric combinations of at least the dimerization domain of the ultraspiracle receptor along with one two or three members of the steroid/thyroid superfamily of receptors including fragments thereof comprising the dimerization domain). Thus the multimeric receptor species of Evans thus anticipate the chimeric protein of claim 1 because it comprises at least two functional protein units wherein each functional unit comprises a dimerization domain, since the linker is optional. The

multimeric receptor could be an endodimer, each multimeric receptor comprises a ligand binding domain, the other limitations are optional, thus claims 2-4 are anticipated. The ultraspiracle receptor is insect derived, thus 5-6 are anticipated. A multimeric receptor comprising the ecdysone receptor is disclosed (column 5, lines 29-30) thus anticipating claims 7-10. A multimeric receptor comprising the dimerization domain of the ultraspiracle protein is disclosed (column 3, lines 27-60) thus claim 11 is anticipated. Multimeric receptors comprising RXR receptors, glucocorticoid receptors, mineralocorticoid receptors etc. are disclosed (column 5, lines 20-46) thus claims 13-14 are anticipated. Since the linker is an optional limitation, claims 15-18 are anticipated. The multimeric receptor would have a C terminal domain, thus claim 19 is anticipated. The hinge domain is optional, thus claims 20-21 are anticipated. The multimeric receptor comprises an activation domain (column 5, lines 47-60), thus claim 22 is anticipated.

Conclusion

6. No claim is allowed.

Advisory Information

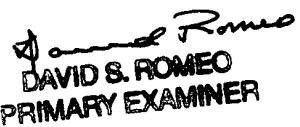
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245. The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
March 4, 2002



DAVID S. ROMEO
PRIMARY EXAMINER